

New algorithm charts evolution of genetic networks during fruit fly life cycle

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A new algorithm developed by Carnegie Mellon University computer scientists has revealed for the first time how genetic networks in the fruit fly, Drosophila melanogaster, evolve during the insect's life cycle.

Scientists have known that the relationships between fruit fly genes change over time, but existing experimental approaches can not capture the details of those changes as they occur. The new algorithm, called Tesla, incorporates machine learning techniques that now enable researchers to figure out how the rewiring of those networks takes place as the insect develops.

"Many problems in biological, social and engineering systems require us to understand the interconnections between genes, people or other entities, but directly observing the evolution of these interconnections has often been impossible because of experimental or computational limitations," said Eric P. Xing, associate professor of computer science, machine learning and language technology in Carnegie Mellon's School of Computer Science. "Researchers typically could identify only a static 'average' network within each system over a period of time, but had no way to capture time-specific 'snapshots' of the actual rewiring network topology at consecutive clock-ticks within the period.

"Our new method exploits the information sharing between the evolving networks, and makes it possible to uncover interconnections that exist for a short moment in time," Xing said. "These findings help us to understand how these networks evolve over time, respond to stimuli and



sometimes become dysfunctional."

In a paper to be published online this week in the Early Edition of the <u>Proceedings of the National Academy of Sciences</u>, Xing and Amr Ahmed, a Ph.D. student in the Language Technology Institute, detail how the Tesla algorithm can be used to analyze not only evolving gene networks in <u>fruit flies</u>, but also changes in voting alliances in the U.S. Senate and shifts in the social network of the machine learning academic community.

"Once we understand the dynamics of a network, we can build models that predict how it will respond to stimuli and identify its vulnerabilities," said Xing, a member of the Ray and Stephanie Lane Center for Computational Biology at Carnegie Mellon. "In the context of cancer genetics, for instance, this dynamic network analysis could help us identify new targets for drug therapy."

In analyzing the gene networks of the fruit fly, Xing and Ahmed began with an existing database that measured the activity of 4,028 genes at 66 intervals spanning the embryonic, larval, pupal and adult periods of the fruit fly life cycle. Each of the samplings, performed with microarrays, provided a snapshot of which genes were active at the time in the large, evolving networks. The Tesla algorithm was used to determine the links between the genes in those networks at the time of the snapshot. Using a novel extension of the sparse regression technique popular in statistical inference, Tesla was able to reverse engineer the rewiring of those links, figuring out exactly how one network related to the next network in the progression. The result is the first "movie" of fruit fly gene network aging.

Because the original data set may have missed important developmental genes, it isn't yet possible to draw any strong biological conclusion from the resulting movie of gene network evolution, Xing said, but the



analysis nevertheless illustrates the promising utility of Tesla.

"To our knowledge, Tesla represents the first practical and scalable method for recovering large-scale, time-varying networks underlying sociocultural and biological processes at arbitrary temporal resolutions," the authors concluded in their report.

Xing and Ahmed also used Tesla to analyze the voting record for 642 bills before the U.S. Senate in 2005 and 2006, and see how relationships between senators changed over time. Democratic and Republican senators tended to bunch together (with then-Sen. Barack Obama always connected only to other Democrats) in their voting, though there were anomalies. For instance, Sen. James Jeffords, then an independent senator from Vermont, had a voting record that was closely tied to Democrats, though around January 2006 his voting began to reflect slightly more connections with the Republicans, his original party. The votes of then-Sen. Lincoln Chafee (R-R.I.) can be seen to progressively change toward the Democrats; he subsequently became an Independent after losing re-election in 2006.

Source: Carnegie Mellon University (<u>news</u> : <u>web</u>)

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